CLIA-waived Rapid HIV Testing in the Public Health Sector

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The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention
Need for Expanding HIV Testing

- 252,000 – 312,000 persons with undiagnosed HIV infection
- ~ 40,000 new HIV infections per year
- ~ 50% of all new sexually transmitted HIV infections are attributed to persons unaware of their infection
- ~ 33% of HIV-infected persons are diagnosed late in the course of their illness
- ARV therapy is of proven benefit clinically and in reducing perinatal HIV transmission
- CDC has supported the use of CLIA-waived rapid tests since 2003 to expand testing to reduce undiagnosed infections, late diagnoses, and perinatal transmission
Presentation Objectives

1. Review the performance of CLIA-waived rapid HIV tests
2. Characterize quality assurance practices and outcomes
3. Describe magnitude of CLIA-waived rapid HIV testing
OraQuick Advance HIV-1/2

FDA-approved claims for:
Sensitivity (HIV-1):
  Whole blood  99.6%  (98.5 - 99.9)
  Oral fluid   99.3%  (98.4 - 99.7)
Specificity (HIV-1):
  Whole blood  100%  (99.7-100)
  Oral Fluid   99.8%  (99.6 – 99.9)
CLIA-waived:
  Whole blood:  Jan 2003
  Oral fluid:   Jul 2004
Uni-Gold Recombigen

FDA-approved claims for:

Sensitivity:
  Whole blood 100% (99.5 - 100)
  Plasma/serum 100% (99.5 -100)

Specificity:
  Whole blood 99.7% (99.0-100)
  Plasma/serum 99.8% (99.3 -100)

CLIA-waived:
  Whole blood: Nov 2004
Clearview HIV-1/2 Stat-Pak

FDA-approved claims for:

Sensitivity (HIV-1):
- Whole blood  99.7% (98.9-100)
- Plasma/serum 99.7% (98.9-100)

Specificity (HIV-1):
- Whole blood  99.9% (99.6-100)
- Plasma/serum 99.9% (99.6-100)

CLIA-waived:
- Whole blood: Nov 2006
Data Sources

1. Four CDC-sponsored studies, 2000-2005
2. Post-marketing surveillance, 2004-2005
Four CDC-sponsored Studies*

Objectives & Methods
- Evaluate performance of OraQuick in settings of likely use
- Performance compared with conventional EIA/WB algorithm
- Subjects included pregnant women at 18 hospitals, and HRH, IDU, and MSM at 41 community outreach sites, 3 HIV tests sites, and 2 STD clinics
- Tests administered by laboratorians, physicians, nurses, midwives, and HIV counselors
- Studies implemented between April 2000 and January 2005

### Sensitivity Results*

<table>
<thead>
<tr>
<th>Rapid Test (Specimen)</th>
<th>Reference Positive</th>
<th>False Negative</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>OraQuick (Whole blood)</td>
<td>327</td>
<td>1</td>
<td>99.7%</td>
</tr>
<tr>
<td>OraQuick (Oral fluid)</td>
<td>327</td>
<td>3</td>
<td>99.1%</td>
</tr>
</tbody>
</table>

### Specificity Results*

<table>
<thead>
<tr>
<th>Rapid Test (Specimen)</th>
<th>Reference Negative</th>
<th>False Positive</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>OraQuick (Whole blood)</td>
<td>12,010</td>
<td>12</td>
<td>99.9%</td>
</tr>
<tr>
<td>OraQuick (Oral fluid)</td>
<td>12,010</td>
<td>54</td>
<td>99.6%</td>
</tr>
<tr>
<td>Conventional EIA</td>
<td>12,010</td>
<td>35</td>
<td>99.7%</td>
</tr>
</tbody>
</table>

False Positive OraQuick Oral Fluid Results, University of Minnesota*

### Observed Specificity

**University of Minnesota***

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Reference Negative</th>
<th>False Positive</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jul 2002 – Apr 2004</td>
<td>2,017</td>
<td>7</td>
<td>99.7%</td>
</tr>
<tr>
<td>Apr 2004 – Aug 2004</td>
<td>388</td>
<td>16</td>
<td>95.9%</td>
</tr>
<tr>
<td>Jul 2002 – Aug 2004</td>
<td>2405</td>
<td>23</td>
<td>99.0%</td>
</tr>
</tbody>
</table>

Investigation & Incidence Study*

Investigation
- 16 false-positive results from unexpired devices from 6 lots
- All lots produced and shipped within specifications
- Each lot used at other sites without excess false-positive results
- All temperatures recorded in device storage and test logs were within manufacturer’s specifications
- Devices had very faint, gray, or shadowy test lines
- Four operators interpreted the results
- Operator practices observed in accordance with PI
- Only significant factor: age ≥ 37 years

Incidence study, Feb-May 2005, 9 cities in 3 states*
- 2,268 tests, no false-positive results (specificity 100%)
- Case-control study could not proceed

Data Sources

1. Four CDC-sponsored studies, 2000-2005
2. Post-marketing surveillance, 2004-2005
Post-marketing Surveillance, 2004-2005*

Objectives
- Evaluate use and performance of OraQuick
- Characterize quality assurance practices and outcomes

Methods
- 17 participating health departments, 368 sites, Aug 2004 – June 2005
- Predominately CTS, STD, outreach, and correctional settings
- Tests administered by counselors and lab techs
- Preliminary positive results subject to WB/IFA confirmation, clients with discordant test results were counseled to re-test.
- Active surveillance of all discordant test results
- False positive results based on initial or repeat WB/IFA confirmation

## Post-marketing Surveillance, 2004-2005*

<table>
<thead>
<tr>
<th>Test and specimen type</th>
<th>No. of Tests</th>
<th>HIV + Median % (range)</th>
<th>Estimated Specificity Median % (range)</th>
<th>PPV Median % (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OQ whole blood</td>
<td>135,724</td>
<td>0.8 (0.1-2.6)</td>
<td>99.98 (99.73-100)</td>
<td>99.2 (66.7-100)</td>
</tr>
<tr>
<td>OQ oral fluid</td>
<td>26,066</td>
<td>1.0 (0.0-4.0)</td>
<td>99.89 (99.44-100)</td>
<td>90.0 (50.0-100)</td>
</tr>
</tbody>
</table>

**Discordant test results**
- Of 124 initially discordant test results: 17 (14%) true positive

**Receipt of test results**
- 94% of non-reactive rapid test results provided
- 95% of reactive rapid test results provided
  - 75% of confirmed results provided

Excess False-positive OF Test Results, 1 San Francisco Test Site*

Investigation*

Findings

- 33 false-positive results from unexpired devices from 4 lots
- Each lot used at 11 other SF sites without excess false-positive results
- 29 (88%) devices had very faint, gray, or shadowy test lines
- Seven operators interpreted the results confirmed by ≥1 other operators
- Operator practices observed in accordance with PI with exception of OF collection (some recommended swabbing gum line ≥ 1 time)
- Operators re-trained in October; 13 (39%) false positive results occurred after re-training
- Of 163 external controls, two were invalid; 161 yielded concordant results
- All temperatures recorded in device storage and test logs were within manufacturer’s specifications

Data Sources

1. Four CDC-sponsored studies, 2000-2005
2. Post-marketing surveillance, 2004-2005
# New York State Anonymous Counseling & Testing Program 2005*

<table>
<thead>
<tr>
<th>Rapid Test (specimen type)</th>
<th>Reference Negative</th>
<th>False Positive</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>OraQuick (whole blood)</td>
<td>13,473</td>
<td>7</td>
<td>99.9%</td>
</tr>
<tr>
<td>OraQuick (oral fluid)</td>
<td>10,077</td>
<td>29</td>
<td>99.7%</td>
</tr>
</tbody>
</table>

*San Antonio-Gaddy M. CDC Presentation, Jan 10, 2007.*
### New York State Anonymous Counseling & Testing Program 2006*

<table>
<thead>
<tr>
<th>Rapid Test (specimen type)</th>
<th>Reference Negative</th>
<th>False Positive</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>OraQuick (whole blood)</td>
<td>3,725</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>OraQuick (oral fluid)</td>
<td>1,838</td>
<td>5</td>
<td>99.7%</td>
</tr>
<tr>
<td>Uni-Gold (whole blood)</td>
<td>16,540</td>
<td>17</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

Presentation Objectives

1. Review the performance of CLIA-waived rapid HIV tests
2. Characterize quality assurance practices and outcomes
3. Describe magnitude of CLIA-waived rapid HIV testing
Post-marketing Surveillance, 2004-2005*

Methods (Practices)
- Administered survey to rapid test program managers:
  - Training requirements
  - Quality assurance monitoring
  - Operator competency assessment
- Limitation: all assessments were made at the program level
Post-marketing Surveillance, 2004-2005*

Methods (Practices)
- Administered survey to rapid test program managers:
  - Training requirements
  - Quality assurance monitoring
  - Operator competency assessment
- Limitation: all assessments were made at the program level

Methods (Outcomes)
- From Jan 2005 – Jun 2005, provided monthly forms and conducted active surveillance of invalid tests, external quality control runs, and temperature violations
Quality Assurance Practices*

Required Training: Median (range)
- 6 (3-16) hrs for operating rapid tests
- 6 (1-40) hrs for counseling rapid-test clients
- 40 (20-80) total hrs for HIV test and counseling “certification”

Training Methods
- 4 (24%) internet or video
- 10 (59%) one-on-one training at rapid test site
- 15 (88%) state, city, or county developed training course
- 2 (12%) CDC rapid test training course
- 6 (35%) other
- 17 (100%) assessed competency in test performance and interpretation of all three types of results
Quality Assurance Practices

Post-training Monitoring
- 15 (88%) visited all test sites during PMS-2 to establish/evaluate QA
- 10 (59%) conducted onsite QA monitoring at least every six months

*Question: Which of the following activities were performed by HD staff for all sites during PMS-2? These QA activities may have been conducted on or off site.
Quality Assurance Practices

Post-training Monitoring

- 15 (88%) visited all test sites during PMS-2 to establish/evaluate QA
- 10 (59%) conducted onsite QA monitoring at least every six months
- 16 (94%) reviewed external QC test procedures*
- 16 (94%) examined test logs*
- 12 (71%) examined temperature logs*
- 8 (47%) observed operators collect specimens*
- 9 (53%) observed operators interpret results*
- 10 (59%) observed how test results were explained to clients*
- 15 (88%) reviewed procedures to address invalid and discordant test results*

*Question: Which of the following activities were performed by HD staff for all sites during PMS-2? These QA activities may have been conducted on or off site.
Quality Assurance Practices*

Internal Competency Assessment
- 10 (59%) conducted at least annual assessments after training
  - 4 used placards with OraQuick test results
  - 4 used blinded external control specimens
  - 2 used samples sent from health department lab

External Competency Assessment
- 13 (76%) enrolled in external assessment program
  - 10 (59%) MPEP
  - 3 (18%) CAP

Quality Assurance Outcomes

Jan-Jun 2005: 86,749 Rapid Tests*

- 20 (0.02%) invalid test results (no control line or red background in results window)
- 9,217 external control runs ~ 10 persons tested/external quality control run (5/17 HDs recommended running daily controls)
- 4 external controls reported as “invalid” (3 health departments)
- 31 (0.06%) site-days where ≥ 1 clients tested when temperature was out of spec (3 health departments)
- 161 (0.32%) site-days where tests stored when temperature was out of spec (5 health departments)

*308 reporting sites; representing ~ 49,896 site-days (308*162) during 6-month reporting period
Presentation Objectives

1. Review the performance of CLIA-waived rapid HIV tests
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Data Sources

3. Selected Health Departments, 2005-2006
Rapid HIV Test Distribution Program

Objectives & Methods

- Implemented to help scale up rapid test programs in support of Advancing HIV Prevention initiative
- 2003-2005: distributed tests to state and local health departments, medical centers, and CBOs
  - Quarterly reports submitted on use of devices
- 2006-2007: distributed tests to state and local health departments in proportion to AIDS morbidity
  - Counseling and testing data sets will be submitted
RTDP 2003-2005

- 790,310 devices distributed
- 121 state/local health depts
- 101 medical centers/CBOs
- 8 correctional facilities
- 230 organizations submitted reports (606,951 devices)
- 372,960 devices used
- 4,650 (1.2%) preliminary positive test results confirmed HIV positive
- 79% of confirmed results given to clients
Devices Distributed

- 37 States, DC, Puerto Rico and US Virgin Islands
- Primarily to moderate and high morbidity areas.
- RTDP July 2006 – June 2007:
  - 211,800 OraQuick devices
  - 59% distributed through Dec 2006

*Human immunodeficiency virus.
†Aged ≥13 years.
§Acquired immunodeficiency syndrome.
Data Sources

3. Selected Health Departments, 2005-2006
Rapid HIV Testing Assessment*

Objectives & Methods

- Evaluate procurement and use of rapid tests
- Questionnaires sent to 65 directly funded health department AIDS program directors and prevention managers
- Survey completed August 2006
- 43 (66%) respondents
  - 39 state health departments
  - 3 city health departments
  - 1 territorial health department

*NASTAD Rapid HIV Testing Assessment Report: www.nastad.org
Support Rapid HIV Test Programs*

Participating Health Departments (n=43)
- 35 (81%) supported a rapid testing program
- 8 did not currently support a program
  - 6 (75%) insufficient resources
  - 2 (25%) statutory or regulatory barriers
  - 4 (50%) will implement program in next 12 months
- 39 (91%) will support program in next 12 months
  - 39 (100%) will continue to use conventional testing
- Settings
  - Outreach (81%), HIV test sites (72%), CBOs (70%)
  - Labor & delivery (26%), Hospital EDs (19%)

*NASTAD Rapid HIV Testing Assessment Report: www.nastad.org
**Projected Purchases, 2006***

<table>
<thead>
<tr>
<th>Quantity of Tests</th>
<th>OraQuick N (%)</th>
<th>Uni-Gold N (%)</th>
<th>Total N</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1,000</td>
<td>2 (6%)</td>
<td>5 (45%)</td>
<td>7</td>
</tr>
<tr>
<td>1,001 – 10,000</td>
<td>17 (55%)</td>
<td>5 (45%)</td>
<td>22</td>
</tr>
<tr>
<td>10,001 – 25,000</td>
<td>7 (23%)</td>
<td>1 (9%)</td>
<td>8</td>
</tr>
<tr>
<td>25,001 – 50,000</td>
<td>4 (13%)</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>50,001 – 75,000</td>
<td>1 (3%)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>31</strong></td>
<td><strong>11</strong></td>
<td><strong>NA</strong></td>
</tr>
</tbody>
</table>

1 Health departments plan to use Uni-Gold exclusively

*Reported by 35 health departments that currently implement rapid testing. NASTAD Rapid HIV Testing Assessment Report: www.nastad.org
# Volume of Rapid and Conventional Testing*

<table>
<thead>
<tr>
<th>Year</th>
<th>Rapid Tests N (%)</th>
<th>Conventional Tests N (%)</th>
<th>Total Tests N</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>445,063 (25%)</td>
<td>1,358,644 (75%)</td>
<td>1,803,707</td>
</tr>
<tr>
<td>2006¹</td>
<td>613,850 (33%)</td>
<td>1,236,382 (67%)</td>
<td>1,850,232</td>
</tr>
</tbody>
</table>

¹Projected

- Projected 37.9% increase in rapid testing
- Projected 9.0% decrease in conventional testing
- Projected 2.6% increase in total testing

*Reported by 39 health departments intending to implement rapid testing in the next 12 months. NASTAD Rapid HIV Testing Assessment Report: www.nastad.org
Data Sources

3. Selected Health Departments, 2005-2006
### NYSDOH ACT Program
**Number of Tests, by Year and Test Type***

<table>
<thead>
<tr>
<th>Year</th>
<th>Rapid OraQuick</th>
<th>Rapid Uni-Gold</th>
<th>Conventional Oral Fluid</th>
<th>Conventional Serum</th>
<th>Total Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>6,581</td>
<td>0</td>
<td>10,261</td>
<td>2,434</td>
<td>19,471</td>
</tr>
<tr>
<td>2004</td>
<td>20,297</td>
<td>0</td>
<td>462</td>
<td>126</td>
<td>20,990</td>
</tr>
<tr>
<td>2005</td>
<td>23,657</td>
<td>0</td>
<td>144</td>
<td>48</td>
<td>23,944</td>
</tr>
<tr>
<td>2006(^1)</td>
<td>3,460</td>
<td>16,540</td>
<td>0</td>
<td>0</td>
<td>20,000</td>
</tr>
</tbody>
</table>

\(^1\)2006 Data is incomplete

- NYSDOH policy is for counselors to offer all testing options to all clients. Conventional testing was available in 2006.

*San Antonio-Gaddy M.  CDC Presentation, Jan 10, 2007.*
# Florida Department of Health
## Number of Tests, by Year and Test Type*

<table>
<thead>
<tr>
<th>Year</th>
<th>Rapid OraQuick</th>
<th>Rapid Uni-Gold</th>
<th>Conventional Oral Fluid</th>
<th>Conventional Serum</th>
<th>Total Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>3,790</td>
<td>0</td>
<td>78,378</td>
<td>219,519</td>
<td>301,687</td>
</tr>
<tr>
<td>2004</td>
<td>23,926</td>
<td>0</td>
<td>63,293</td>
<td>208,383</td>
<td>295,602</td>
</tr>
<tr>
<td>2005</td>
<td>34,780</td>
<td>0</td>
<td>54,745</td>
<td>200,020</td>
<td>289,545</td>
</tr>
<tr>
<td>2006¹</td>
<td>47,000</td>
<td>0</td>
<td>49,460</td>
<td>192,668</td>
<td>289,128</td>
</tr>
</tbody>
</table>

¹Projected

- Projected 37% decrease in conventional oral fluid testing 2003 through 2006
- Projected 12% decrease in conventional serum testing, 2003 through 2006

*Marlene LaLota, Florida Department of Health, personal communication, 02/08/2007.
Conclusions

CLIA-waived Rapid HIV Tests

- Provided by most health departments; use has increased remarkably
- Stored and used in accordance with the manufacturer’s guidelines, including use on external quality controls
- Accurate, safe, and simple to use
- Enabled nearly all clients to receive their results
- Helped to expand testing, enabling HIV diagnoses of persons who might not have had their infections diagnosed otherwise
Conclusions

CLIA-waived Rapid HIV Tests

- Despite high specificity, positive predictive value can be low in some settings
- Clusters of excess false-positive test results have occurred and may continue to occur
- Many persons with preliminary positive test results do not return to the clinic to receive their confirmed results
- Need to evaluate the feasibility and performance of a POC rapid test algorithm to improve accuracy of results and linkage to care
Research Needs

Rapid Test Algorithm Study

- Collaborators: Departments of Health, San Francisco and Los Angeles
- Status: Protocol under development
- Expected start date: Spring, 2007
- Sites: multiple rapid test sites in SF and LA
- Methods:
  - Intervention sites: screen with OraQuick on oral fluid, if reactive, repeat in series with Uni-Gold and Stat-Pak
  - All clients with reactive OQ results undergo conventional WB/IFA confirmation
  - All clients with discordant WB/IFA results are followed
  - Evaluate % who use health-care from intervention and control sites
Questions